**Supplemental Material**

Approach for Generating Alternative/Simulated Exposure Levels in an Occupational Cohort for Use in an Uncertainty Analysis

Supplemental Material for "A Constrained Maximum Likelihood Approach to Evaluate the Impact of Dose Metric on Cancer Risk Assessment: Application to β-Chloroprene," Allen et al.

A cohort of individuals studied by Marsh *et al*. (2007a) was included as part of the analysis of cancer risk associated with β-Chloroprene (CD) exposure in the above-referenced manuscript. The cohort that worked at the Louisville, KY plant was characterized with respect to historical exposure levels. The analysis included an uncertainty analysis (specifically focused on uncertainties associated with such exposure reconstruction). A Monte Carlo approach was used to generate alternative/simulated exposure levels that then could be used for dose-response assessment. The process used to generate the simulated data is described below.

Table S1 shows the break-down of the cohort with respect to job class and job subtitle. In that table, JC = job class, JS = job subtitle (within JC), and JT = job task (within JS) (only available for some JS's, e.g., L7, Operators; these are in comments column of Table S1).

A worker may have a series of JC assignments during the course of his employment. To generate a simulated exposure for that individual in one of those JC's, the following procedure was followed:

1. Randomly pick a JS for that JC.

2. If the rotation type for that JS is "None," then do estimation of exposure level (see below) and keep that estimate of exposure until the JC assignment changes (or end of employment is reached) **or** a time point is reached where the nominal level for the JC changes or the GSD changes (Tables S2, S3 and S4).
3. If the rotation type for that JS is "Equitable" and there are no JT's listed for that JS, then do the estimation of exposure level (see below) every month. Since nominal levels and GSD change by year, the monthly changes were assumed to coincide with the first of every calendar month (meaning that some parts of the duration of the JC assignment, at its beginning and/or at the end, will not be full months).
4. If the rotation type for that JS is "Equitable" and there are JT's listed for that JS, then:
    a. pick a set of Betas and assign them to the JT (as per procedure below)
    b. do the estimation of an exposure level for each JT
    c. compute weighted average exposure
    d. repeat a-c every month (see note in case 3 above about monthly changes occurring at the first of every calendar month)
5. If the rotation type is "Random A" or "Random B" then do estimation of exposure level once and keep that estimate of exposure until the JC assignment changes (or end of employment is reached **or** a time point is reached where the nominal level for the JC changes or the GSD changes (Tables S3 and S4). This will differ from case 2 above in the choice of Q, the mode of the triangular distribution, where here Q = 0.25 for Random A and Q = 0.75 for Random B.

Estimation of exposure level:

Let

nel = nominal exposure level for JC and year in question (Tables S2 and S3) (Esmen *et al.* 2007a)

GSD = geometric standard deviation for year in question (Table S4)

Let $d_L$ and $d_H$ be the deciles associated with the JS or JT in question ($d_L$ may equal 1 and $d_H$ may equal 10, and those are the default values when deciles are not specified in Table S1).

Pick u from a U(0,1) distribution

$$u' = (d_L\text{-}1)/10 + u*(d_H - (d_L - 1))/10$$

For Let F(x) = u', find x from inverse triangular distribution. If rotation type = "None" or "Equitable" then Q (the mode of the triangular distribution) equals 0.5. If rotation type is "Random A" then Q = 0.25. If rotation type is "Random B" then Q = 0.75, with minimum=0 and maximum=1 for all cases.

Finally, exposure level = exp{ln(nel) – 2*ln(GSD) + x*(4*ln(GSD))}. Note that this analysis uses a triangular distribution instead of a lognormal distribution to limit the extremes of exposure estimation. The triangular distribution's endpoints are ln(nel) $\pm$ 2*ln(GSD) (on the log-scale), so the extreme low and high exposures that could be generated (at random) from an unconstrained lognormal distribution are eliminated.

Estimation of Betas (weights to use with the subtasks for equitable job codes with multiple subtasks) are calculated using the following steps:

- Choose a value for each of the n Betas using a U(1,30) distribution representing the number of days in the month, where n is the number of subtasks in the group
- Rescale the n Betas by dividing by the sum of the beta values so that all values are between 0 and 1 and the sum of the betas = 1.

This method has the following features:

- Randomly assigning the betas to the subtasks is not necessary as they are already in a random order so can be assigned on a one-to-one basis.
- All subtasks are represented in each month.

After all individuals in the cohort have been reassigned exposure estimates for each time period associated with a job class and subtitle, the cohort data is analyzed using the OCMAP software (Marsh *et al.* 1998) to generate new estimates the quartile-specific and overall average cumulative exposure.

740 Table S1. Louisville Job Classes (JC), Subtitles (JS), and Job Assignment Structure

| JOB CLASS & SUBTITLES | JC | Rotation | Deciles | Comments |
|---|---|---|---|---|
| **Background** | **L1** | | | |
| Administration | | None | | |
| Food Service | | None | | Probably lower than administration |
| Background | | None | | |
| **Plant Maintenance & Labor** | **L2** | | | Maintenance has only intermittent exposures |
| Carpenters | | None | 1 – 4 | Usually not exposed |
| Non-chemical operators (A) | | Random A | 1 – 4 | |
| Laborers (A) | | Random A | 3 – 10 | |
| Electricians | | None | 1 – 10 | |
| Service Operators | | None | 1 – 10 | Usually exposed but level indeterminate |
| Pipefitters | | None | 1 – 10 | |
| Laggers | | None | 1 – 10 | |
| Shipping/Stores (B) | | Random B | 4 – 8 | |
| Painters (B) | | Random B | 1 – 5 | |
| Firemen (B) | | Random B | 1 – 5 | |
| Transportation (B) | | Random B | 6 – 10 | |
| Mechanics | | None | 1 – 10 | Some not exposed some as service operator. |
| Foremen | | None | 1 – 10 | |
| Boilermakers | | None | 1 – 10 | |
| Supervisors | | None | 1 – 4 | |
| Engineers | | None | 2 – 7 | |

| JOB CLASS & SUBTITLES | JC | Rotation | Deciles | Comments |
|---|---|---|---|---|
| Control Room | | None | 1 – 4 | |
| **Power Services** | **L3** | | | |
| Power Operators & Helpers | | Equitable | 1 – 5 | |
| Boiler Firemen | | Equitable | 4 – 10 | |
| HCL Operators | | Equitable | 3 – 8 | |
| Incinerator Operators | | Equitable | 6 – 10 | |
| **Laboratory** | **L4** | | | |
| Laboratory Technician | | Equitable | 8 – 10 | |
| Laboratory Attendant | | Equitable | 6 – 10 | |
| Laboratory Dishwasher | | Equitable | 1 – 8 | |
| Chemist | | None | 1 – 10 | |
| **MVA** | **L5** | | | |
| Operators | | Equitable | | Inside (1-2):Outside (2-6) Sampling (6-8) Maintenance or repair (1-10) : Rotates with Chemical Operator |
| Foremen | | None | 1 – 4 | |
| Helpers | | Equitable | | 2 Helpers per operator one inside one outside. Clean up (7-10) Inside (1-2) Outside (2-6) |
| Chemical operators | | Equitable | | Same as operator |
| **Monomer** | **L6** | | | |
| Operators | | Equitable | | Inside (1-2):Outside (2-6) Sampling (6-8) Filters (8-10) Shipping (2 – 4) Maintenance or repair (1-10) |

| JOB CLASS & SUBTITLES | JC | Rotation | Deciles | Comments |
|---|---|---|---|---|
| Foremen | | None | 2 – 4 | |
| Supervisors | | None | 1 – 2 | |
| Monomer Helpers | | Equitable | | Clean up (7-10) Inside (1-2) Outside (2-6) Filters(8-10) |
| **Polymer** | **L7** | | | |
| Operators | | Equitable | | Clean up (7-10) Kettle (8 - 10) 3rd Floor - Feed and additives (1 - 3) Basement (2 – 6) Filters (2-6) |
| Foremen | | None | 3 – 7 | |
| Supervisors | | None | 1 – 4 | |
| **Polymer Cleanup Operators** | **L8** | | | |
| Cleanup | | Equitable | 2 – 10 | |
| Utility | | Equitable | 1 – 6 | |
| High Pressure Water | | Equitable | 6 – 8 | |
| **Freon** | **L9** | | | |
| All jobs | | None | | |
| **Finishing** | **L10** | | | |
| Baggers | | Equitable | 6 – 10 | |
| Finishing | | Equitable | 6 – 10 | |
| Packaging | | Equitable | 1 – 4 | |
| Ropers | | Equitable | 3 – 7 | |
| Dryers | | Equitable | 3 – 7 | |
| Choppers | | Equitable | 1 – 6 | |
| Mill Room | | Equitable | 1 – 6 | |

| JOB CLASS & SUBTITLES | JC | Rotation | Deciles | Comments |
|---|---|---|---|---|
| **Freon Mechanics** | **L11** | | | |
| All jobs | | None | | |

741 a Deciles of the distribution varying exposure levels associated with the subtitle.

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743 Table S2: Uniform Exposure Classification Levels

| Exposure Class | Chloroprene Monomer[a] | |
|---|---|---|
| | Exposure Range | Nominal Exposure |
| 0 | Exposure < 0.0005 | 0 |
| 1 | 0.0005–0.005 | 0.0016 |
| 2 | 0.005–0.05 | 0.016 |
| 3 | 0.05–0.5 | 0.16 |
| 4 | 0.5–5 | 1.6 |
| 5 | 5–50 | 16 |
| 6 | 50–100 | 71 |
| 7 | >100 | 160 |

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745 [a] Nominal exposure level (ppm).

746 Obtained from Esmen et al. (2007a) Table 2

747 Table S3: Summary of estimated chloroprene monomer exposure class levels for Louisville

748 Plant

| Year /Job classes | L1 | L2 | L3 | L4 | L5 | L6 | L7 | L8 | L9 | L10 | L11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Pre-1955 | 1 | 5 | 3 | 5 | 5 | 5 | 6 | 6 | 0 | 6 | 0 |
| 1955–1957 | 1 | 4 | 3 | 5 | 5 | 5 | 5 | 5 | 0 | 5 | 1 |
| 1958–1960 | 1 | 4 | 3 | 4 | 5 | 5 | 5 | 5 | 0 | 5 | 1 |
| 1961–1963 | 1 | 4 | 3 | 4 | 5 | 4 | 5 | 5 | 0 | 5 | 1 |
| 1964–1974 | 1 | 4 | 3 | 4 | 4 | 4 | 5 | 5 | 0 | 5 | 1 |
| 1975 | 1 | 4 | 3 | 4 | 3 | 4 | 5 | 5 | 0 | 5 | 1 |
| 1976 | 1 | 4 | 3 | 4 | 3 | 4 | 5 | 5 | 0 | 4 | 1 |
| 1977–1979 | 1 | 4 | 3 | 4 | 0 | 4 | 5 | 5 | 0 | 4 | 1 |
| 1980 | 1 | 4 | 3 | 3 | 0 | 4 | 4 | 4 | 0 | 4 | 1 |
| 1981–1986 | 1 | 3 | 3 | 3 | 0 | 4 | 4 | 4 | 0 | 4 | 1 |
| 1987–1990 | 1 | 3 | 2 | 3 | 0 | 4 | 4 | 4 | 0 | 3 | 1 |
| 1991 | 1 | 2 | 2 | 3 | 0 | 4 | 4 | 4 | 0 | 3 | 1 |
| 1992 | 1 | 2 | 2 | 3 | 0 | 4 | 4 | 4 | 0 | 2 | 1 |
| 1993–1996 | 1 | 2 | 2 | 3 | 0 | 3 | 4 | 3 | 0 | 2 | 1 |
| Post-1997 | 1 | 2 | 2 | 3 | 0 | 3 | 3 | 3 | 0 | 2 | 1 |

749 Obtained from Esmen et al. (2007a) Table 3, where Job classes included:

750 L1 - Background Administration, food service, other external jobs

751 L2 - Plant maintenance and labor Trades, service operators, shipping stores, outside labor

752 L3 - Power services Power, HCl, incinerator operators and helpers

L4 - Laboratory chemist, technician, attendant

L5 - MVA Operators, helpers

L6 - Monomer Operators, helpers, foremen

L7 - Polymer Operators, helpers, foremen

L8 - Polymer cleanup Clean-up, utility, high pressure water operators and helpers

L9 - Freon (all jobs)

L10 - Finishing Baggers, ropers, dryers, choppers, mill room

L11 - Freon mechanics Freon mechanics

761 Table S4: Observed Reduction of Geometric Standard Deviation By Year with Resulting

762 Piecewise Linear Formula for Yearly Changes

| **Year** | **Observed Range ($\sigma_G$)** |
|---|---|
| 2000 - 1991 | 1.75 - 2.25 |
| 1990 - 1987 | 2.0 - 2.5 |
| 1986 - 1984 | 2.25 - 2.75 |
| 1983 - 1982 | 2.5 - 3.0 |
| 1982 - 1981 | 2.75 - 3.25 |
| 1980 | 3.0 - 3.5 |
| 1979 | 3.25 - 3.75 |
| 1978 | 3.5 - 4.0 |
| 1977 | 3.75 - 4.25 |
| 1976 | 4.0 - 4.5 |
| 1975 | 4.25 - 4.75 |
| 1974 - 1966 | 4.5 - 5.0 |
| 1965 or earlier | 4.75 - 5.25 |
| Equation for GSD ($\sigma_{G_i}$) point estimate: $\sigma_i^2 = \sigma_{i+1}^2 + \sigma_w^2 \times \frac{\Delta\sigma^2}{year}$ where i denotes a year, $\sigma_w^2$ = 0.1685, $\sigma_{2000}^2$ = 0.345, and $\sigma_{G_i} = e^{\sigma_i}$ | |

| Year | $\Delta\sigma^2/year$ |
|---|---|
| 2000 - 1995 | 0 |
| 1994 - 1984 | 0.183 |
| 1983 - 1974 | 0.966 |
| 1973 - 1964 | 0.091 |
| 1963 - 1957 | 0.041 |
| 1956 - 1946 | 0.029 |

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